DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
1401 Rockviile Pike
Rockville MD 20852-I 448

Our Reference No.: 99-0884

June 6, 2000

Dawn M. Viveash, M.D.
Immunex Corporation
51 University Street
Seattle, Washington 98 10 l

Dear Dr. Viveash:

Your request to supplement your biologics license application for Etanercept to expand the indication to include reducing the signs and symptoms and delaying structural damage in patients with moderately to severely active rheumatoid arthritis, including those who have not previously failed treatment with a DMARD, has been approved. The revised labeling also includes updated efficacy and safety data regarding Polyarticular-course Juvenile Rheumatoid Arthritis (JRA) and changes to the patient package insert.

We acknowledge your written commitments of May 12, 2000 and June 5, 2000, which include the following:

1. To obtain yearly x-rays on the patients from Protocol 16.0012 who initially received and continued on the 25 mg dose of Enbrel. The x-rays will be obtained for five years and results submitted to ——— annually beginning December 2000 and continuing through December 2003.

2. To obtain long-term data on the development of cancer and autoimmune diseases for all patients who are enrolled in protocols 16.0018 (long-term follow-up study from prior RA and JRA studies) and 16.0023 (long-term follow-up study for patients enrolled in protocol 16.0012). Data on development of cancer and autoimmune diseases will be obtained periodically including at three, five, and ten-year time points. ———————————————————

3. To assess quarterly the cell culture fermentation failure rate due to microbial contamination attributable to aseptic integrity failure of the ——— fermenters for the previous six months and to promptly notify FDA if the failure rate exceeds —— . . If a —— failure rate occurs prior to the end of a quarter, you will notify FDA immediately and discuss with the Agency the corrective actions to be implemented based on their ability to decrease the contamination rate and increase the aseptic integrity. These corrective actions will include designating a specified time for expansion of the pressure hold testing to include piping associated with the —— and —— fermenters where the expansion does not lead to a greater risk for contamination. In addition, ———————— media fills, specialized operator training, replacement of specific equipment and valves, etc., will be evaluated.

Please note that although-data regarding the efficacy of Enbrel as measured by _____ _____ and the percentages of patients with no increase in erosion scores are not described in the package insert for Enbrel, the agency does-not object to Immunex conveying these results in its communications so long as they are presented in a fair and balanced manner. However, it is inappropriate based on available data to make claims of superiority of Enbrel to methotrexate.

Please submit final printed labeling at the time of use and include implementation information on FDA Form 2567. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2567 or Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

This information will be included in your biologics license application file.

Sincerely yours,

Karen D Weiss

K&en D. Weiss, M.D.
Director
Division of Clinical Trial
Design and Analysis
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research